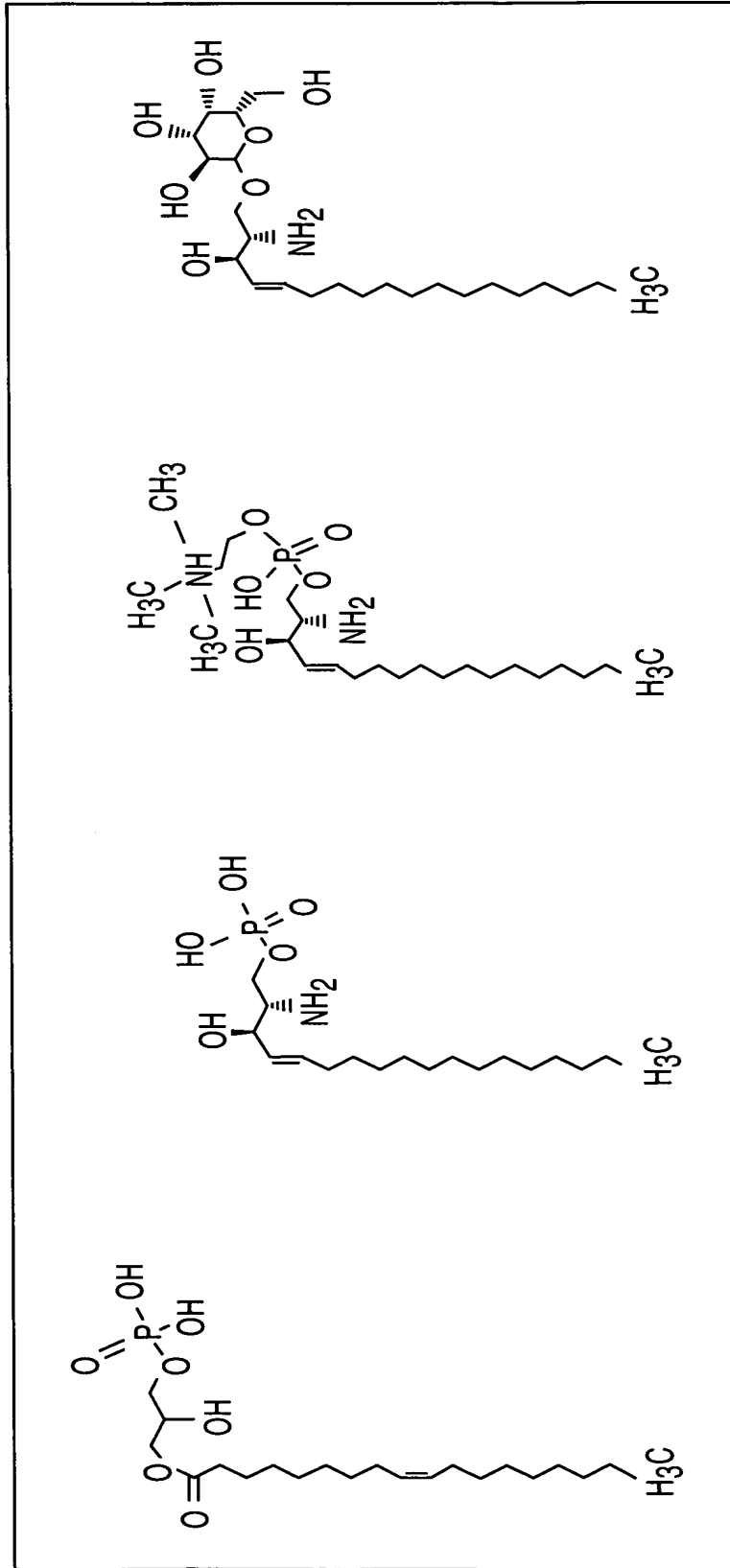




Fig.1A



LPA

S1P

SPC

Psychosine

Fig.1B

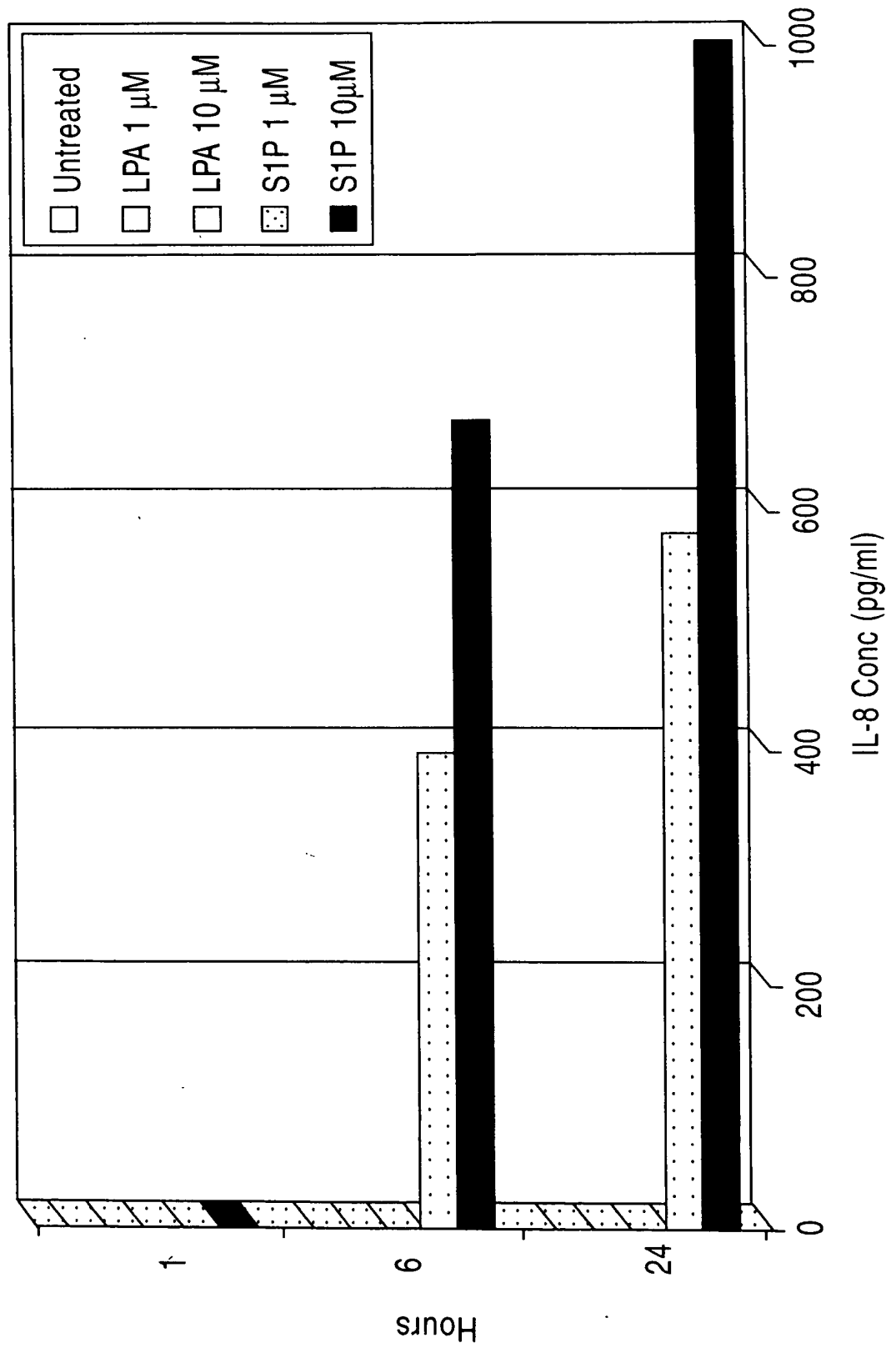


Fig.2A

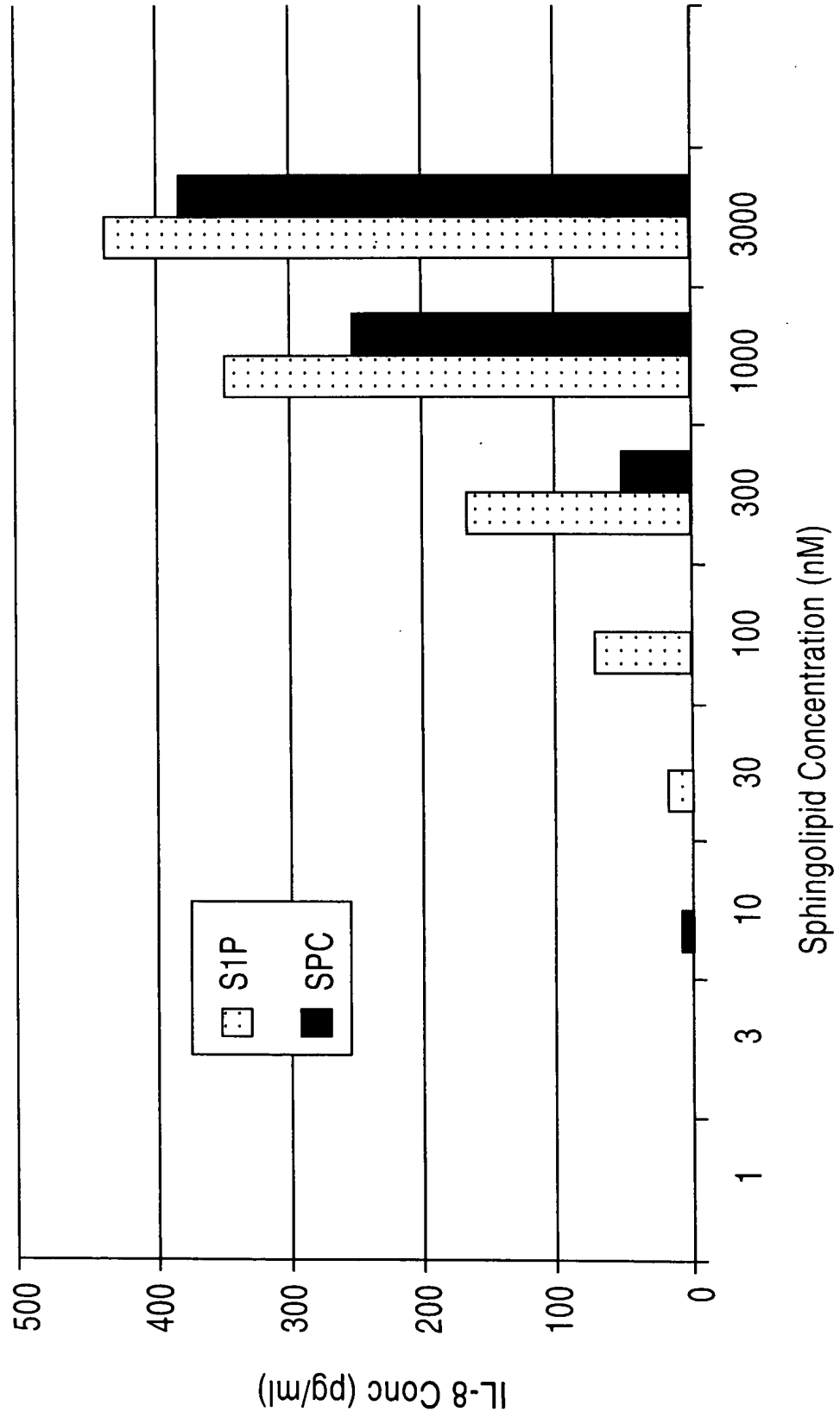


Fig.2B

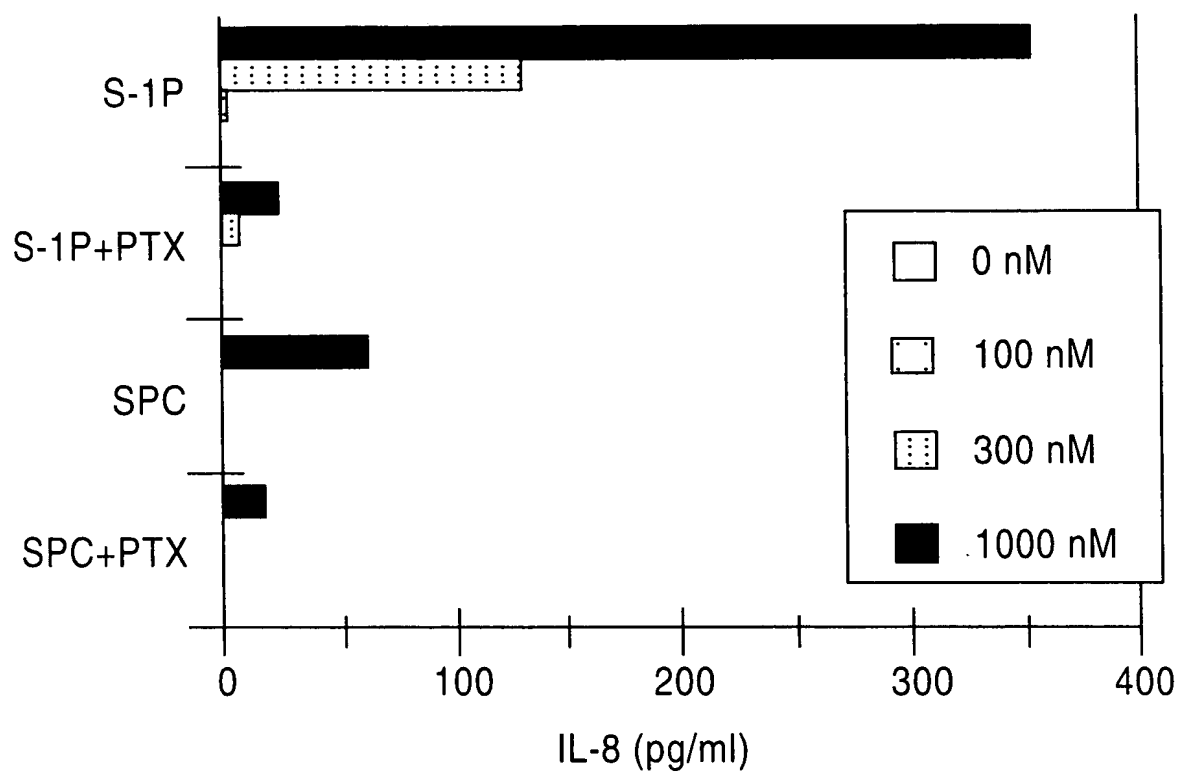


Fig.3

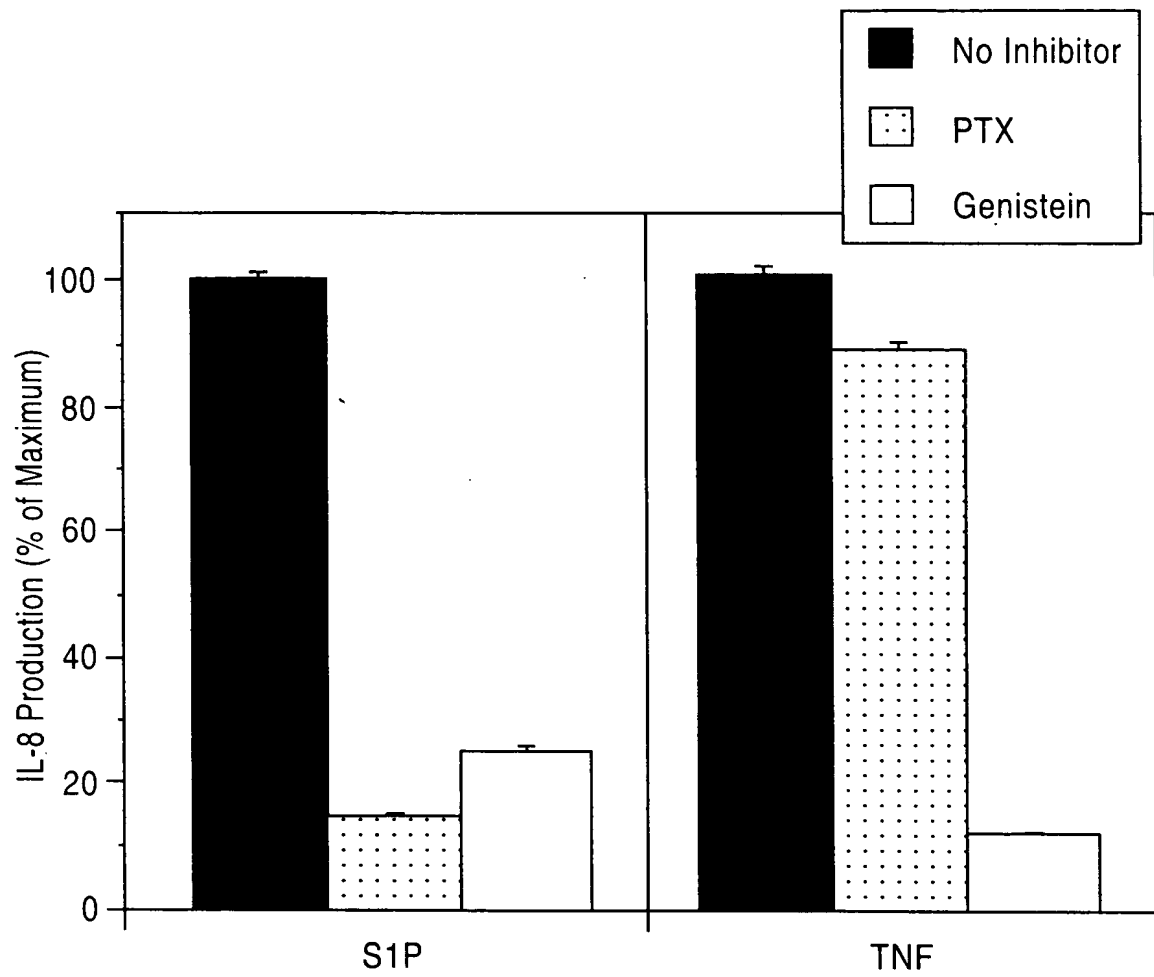


Fig.4A

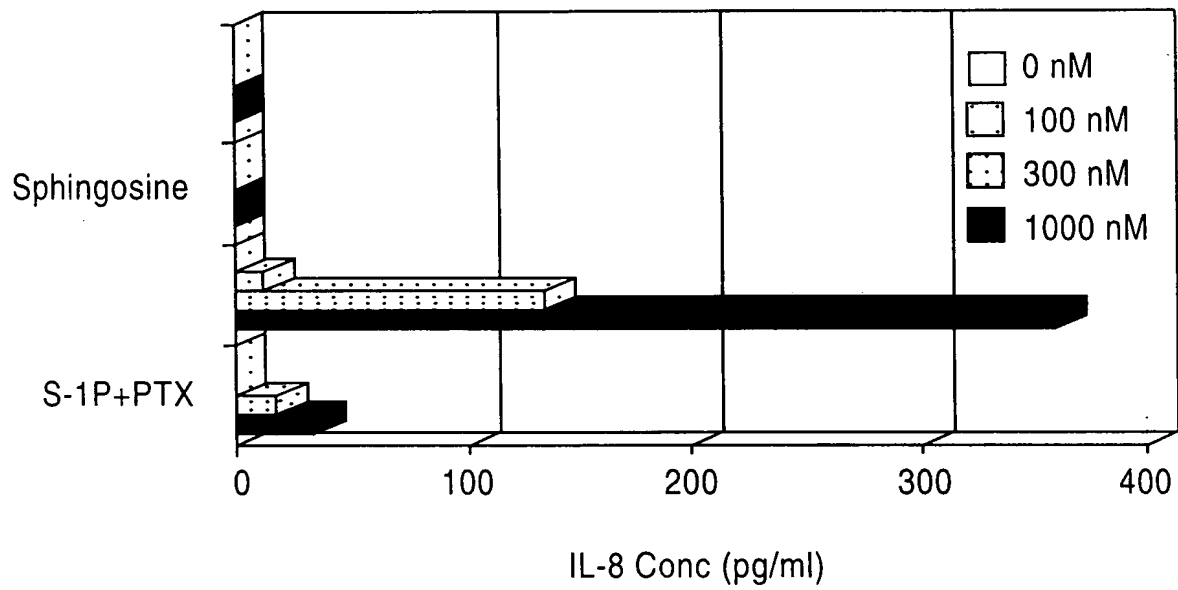


Fig.4B

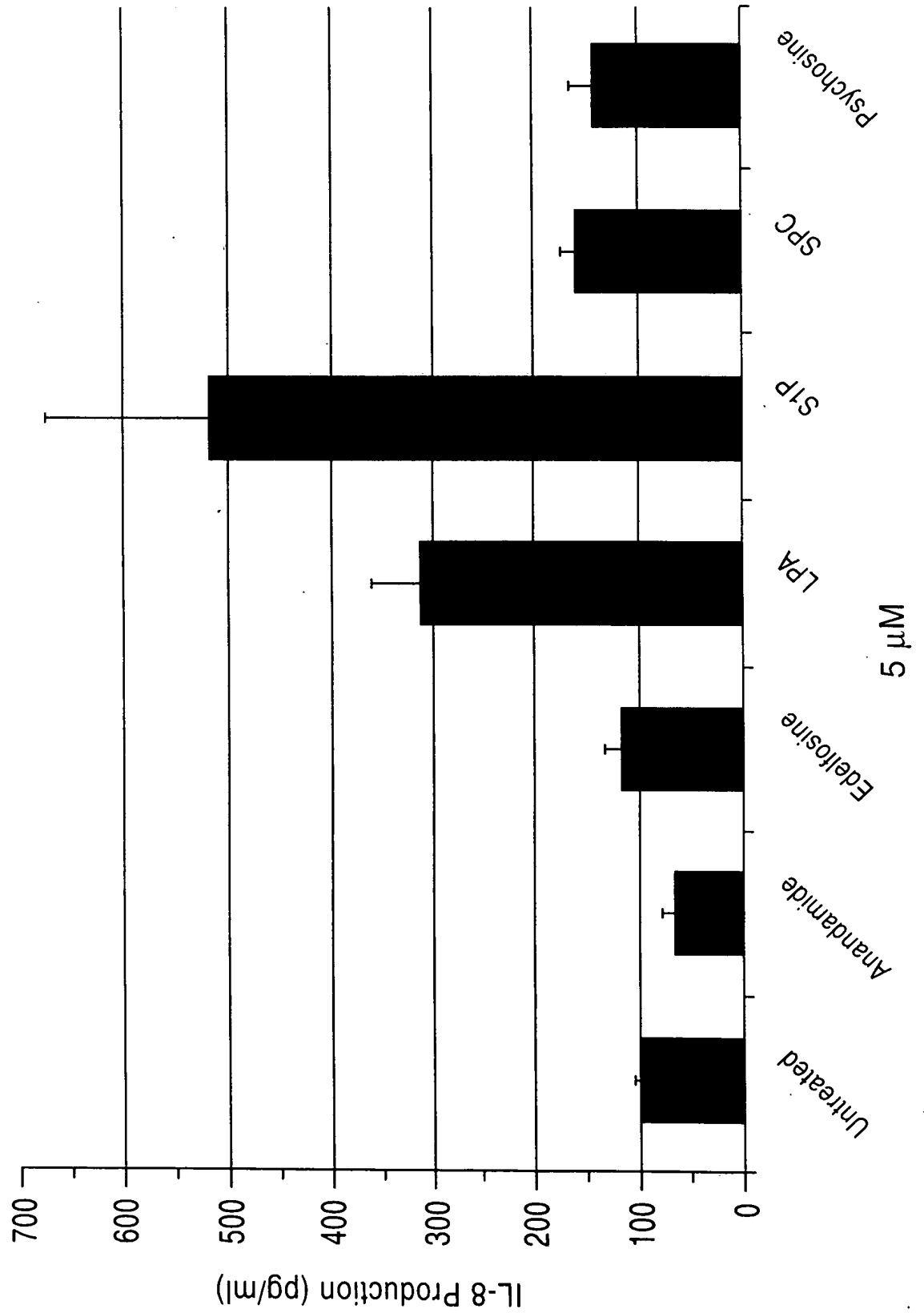
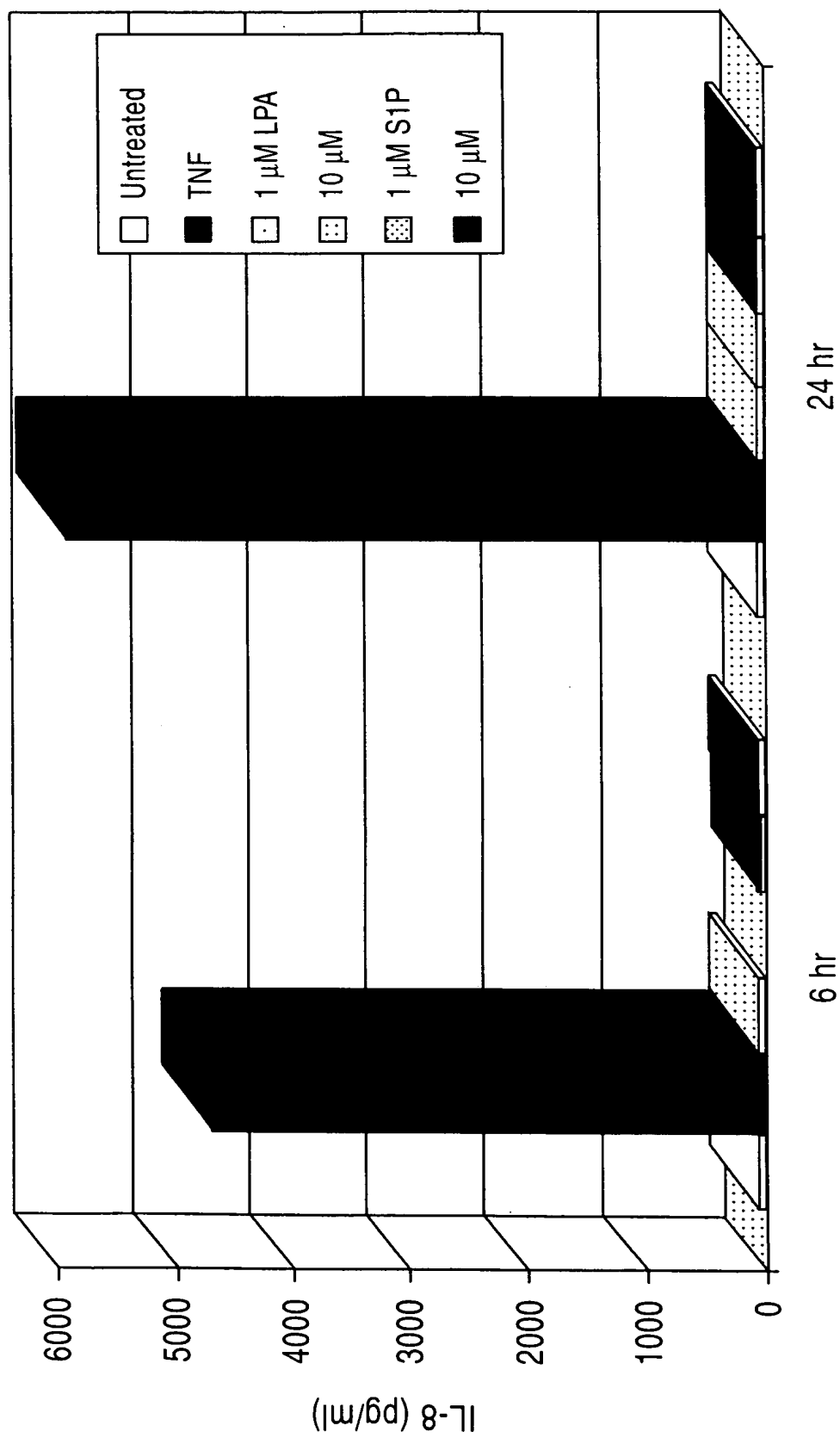


Fig.5





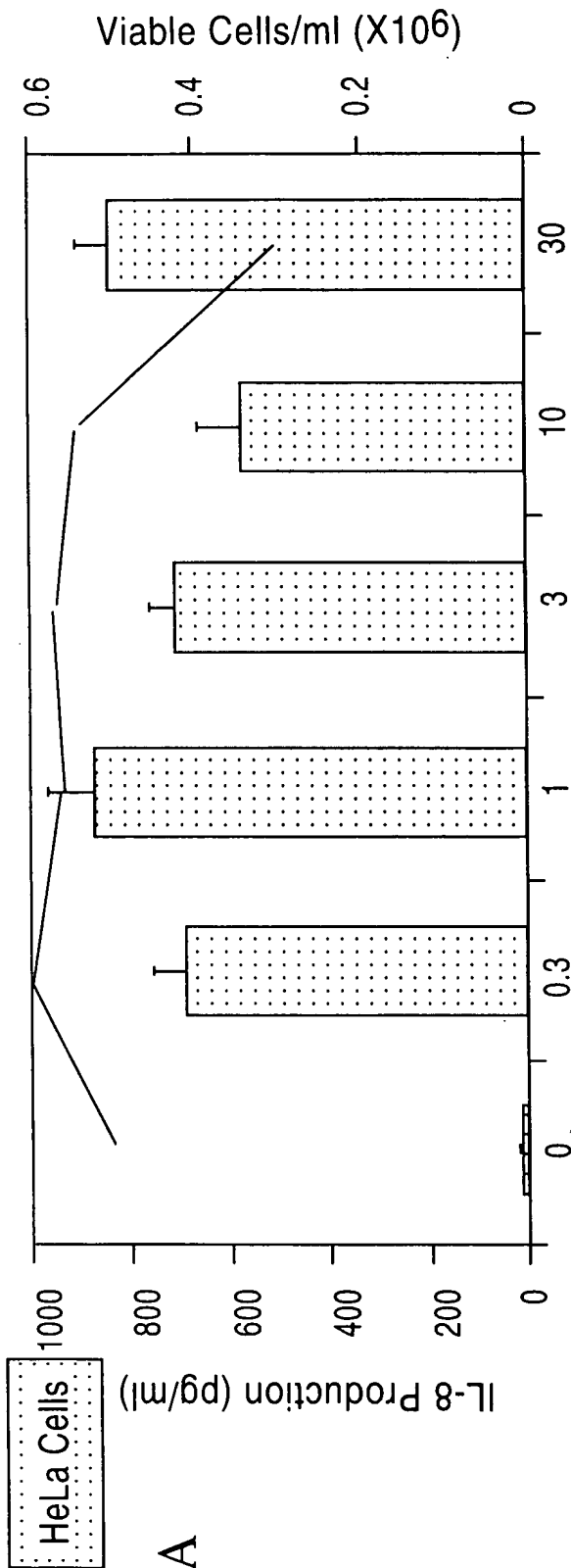


Fig.6A

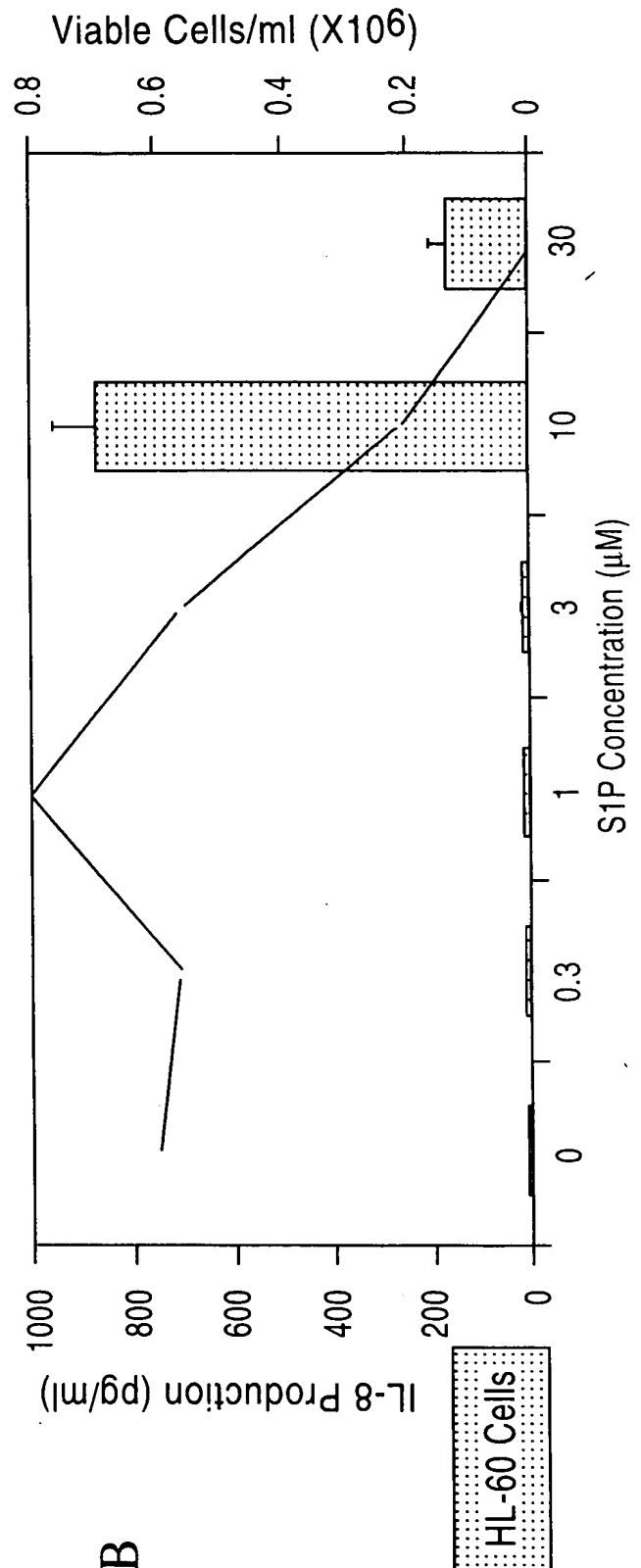
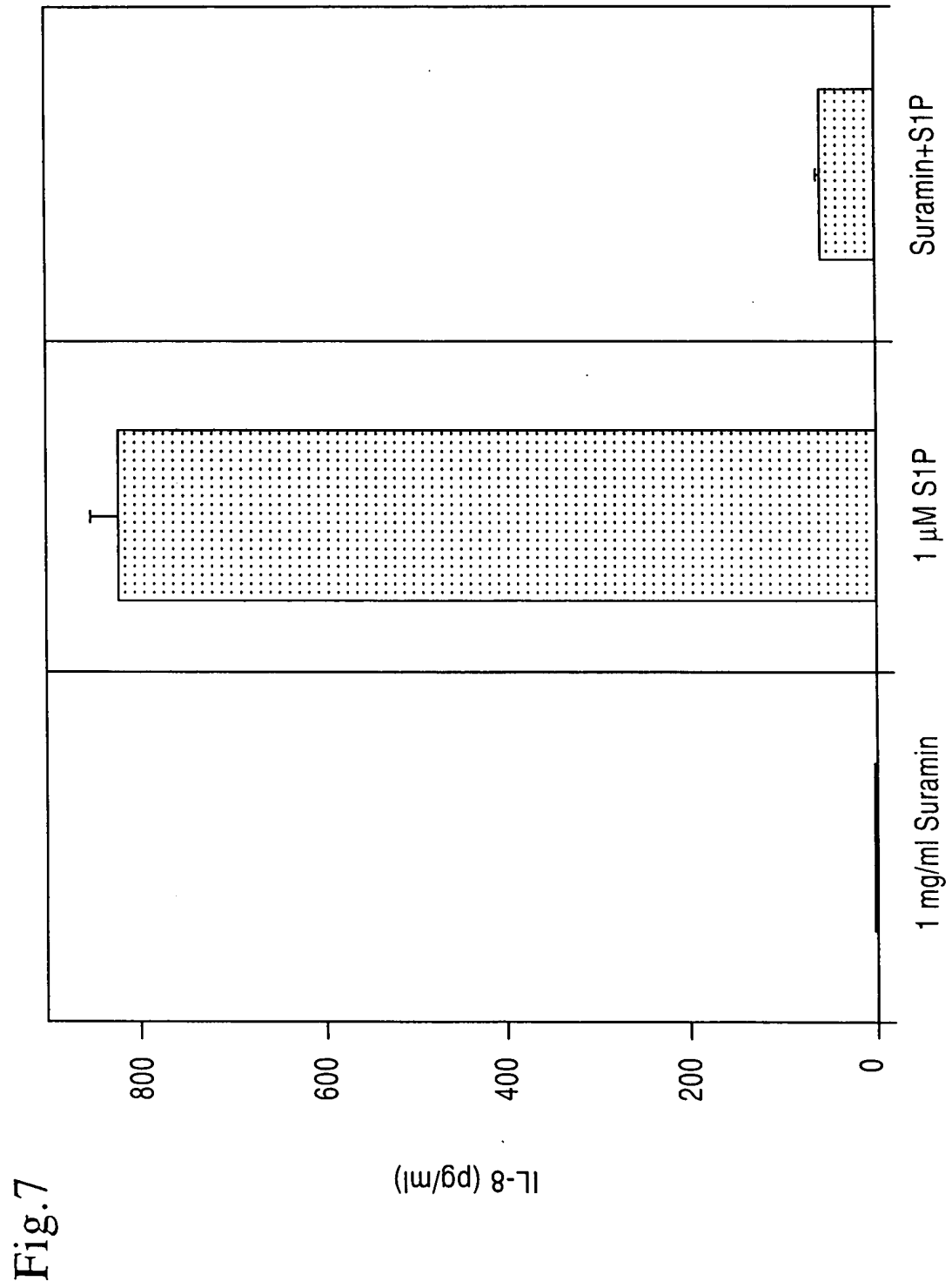


Fig.6B



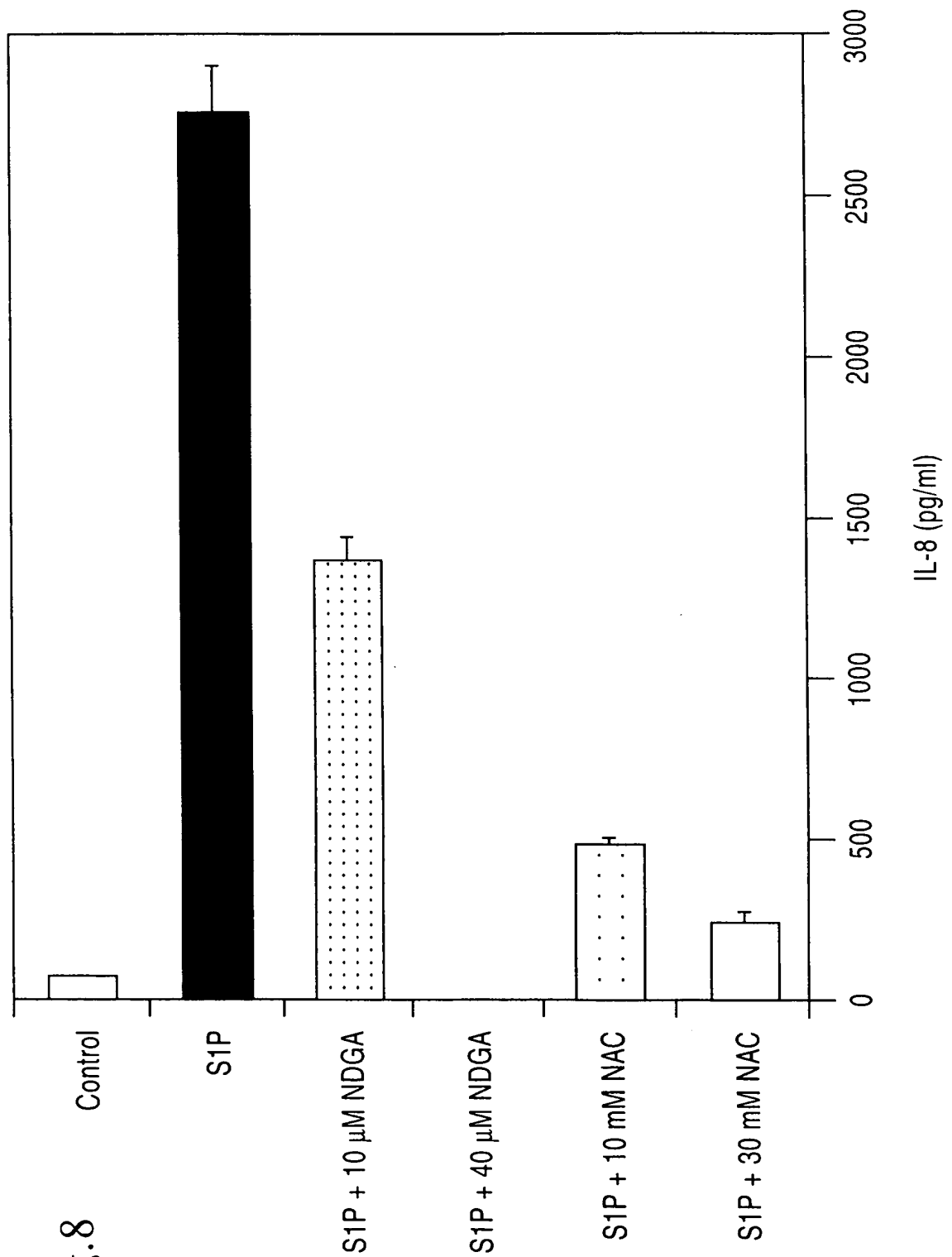


Fig.8

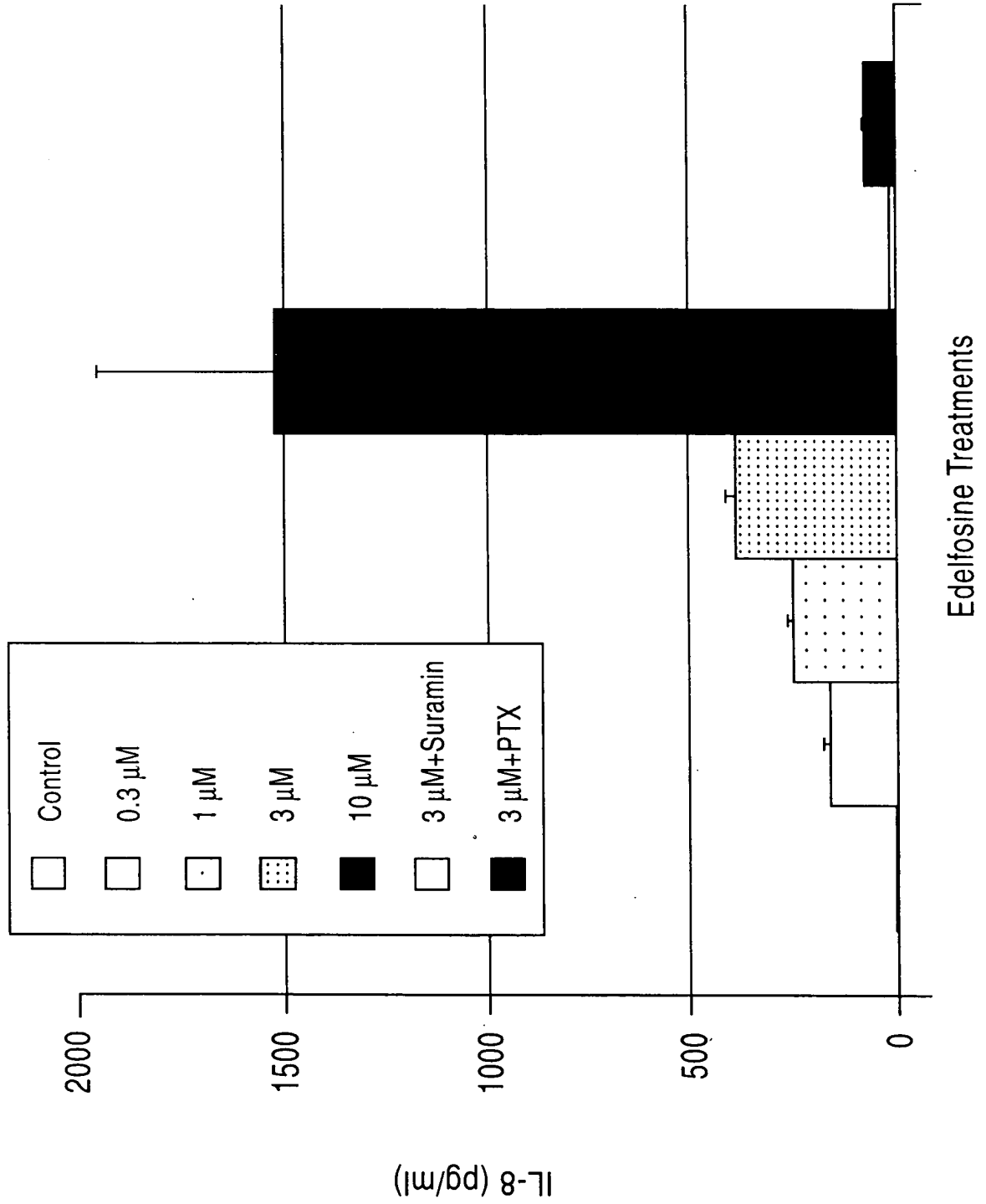


Fig.10A

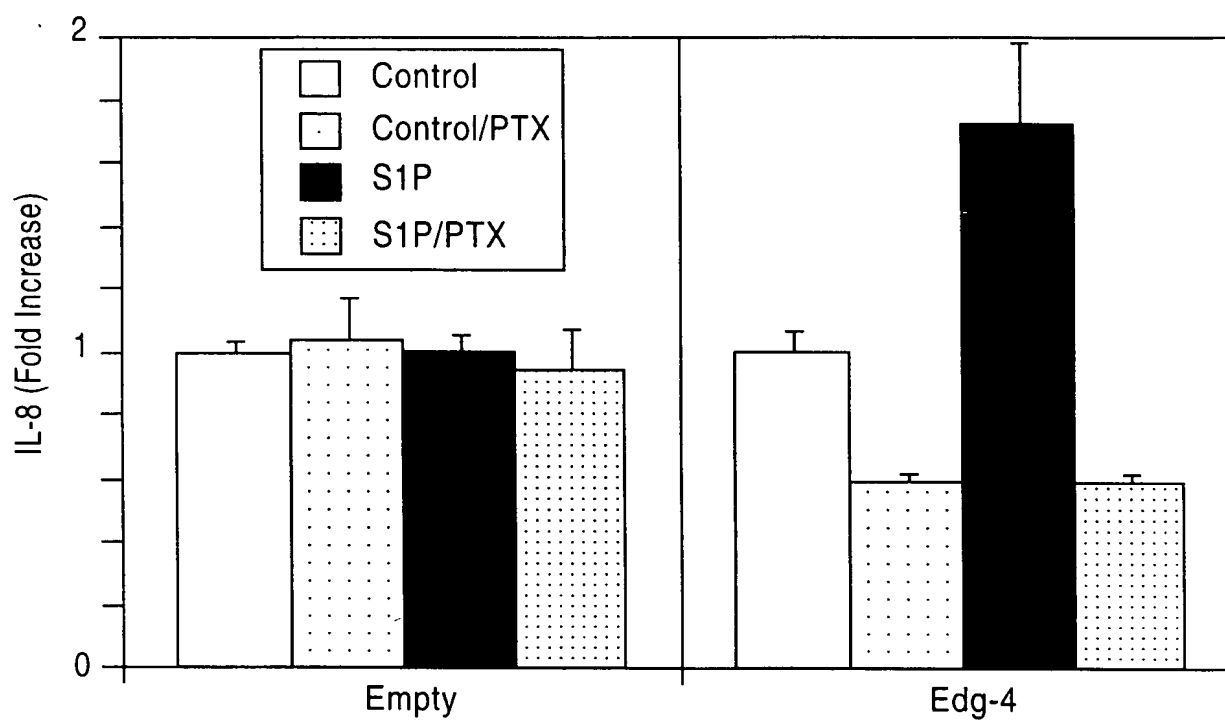


Fig.10B

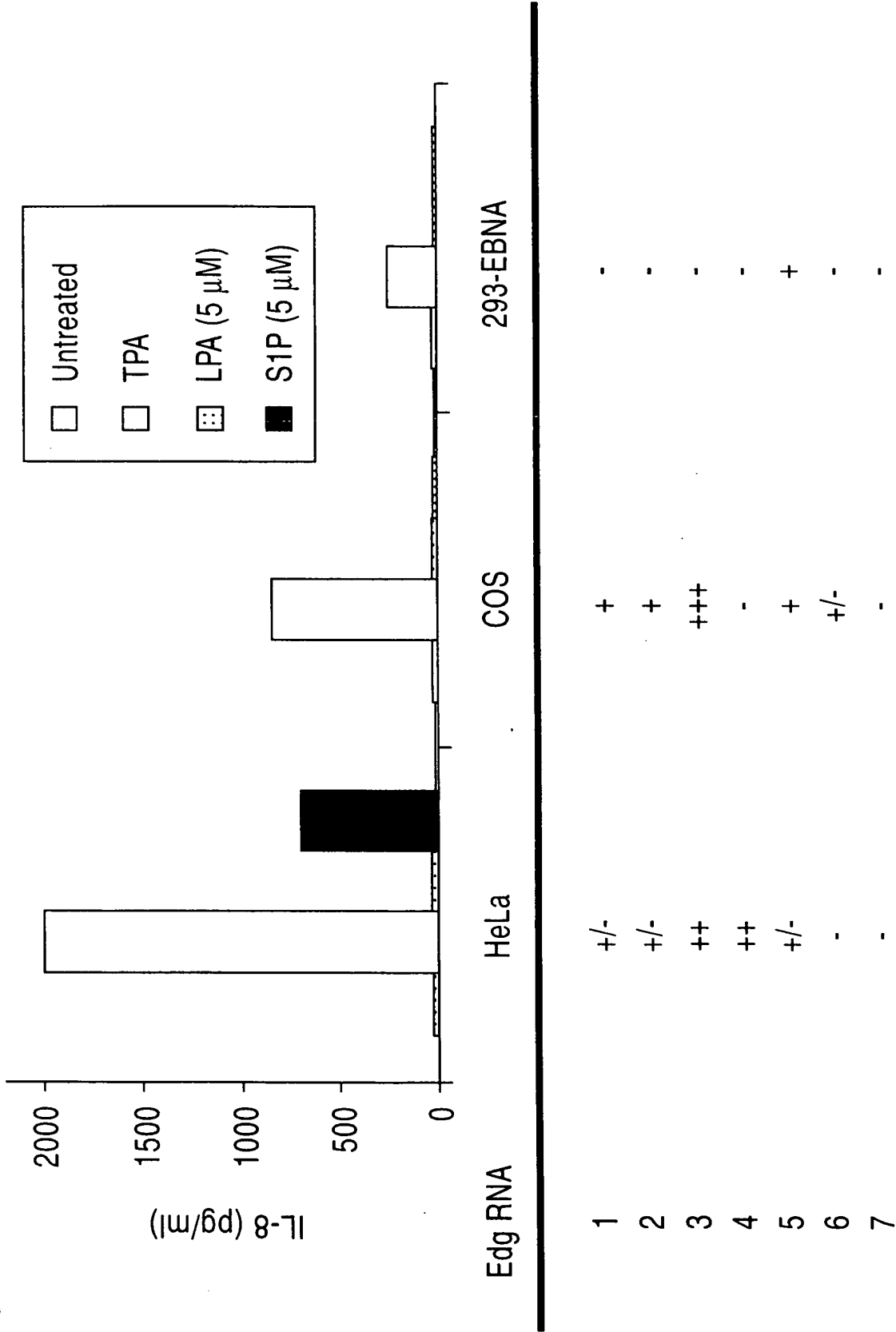


Fig.11B

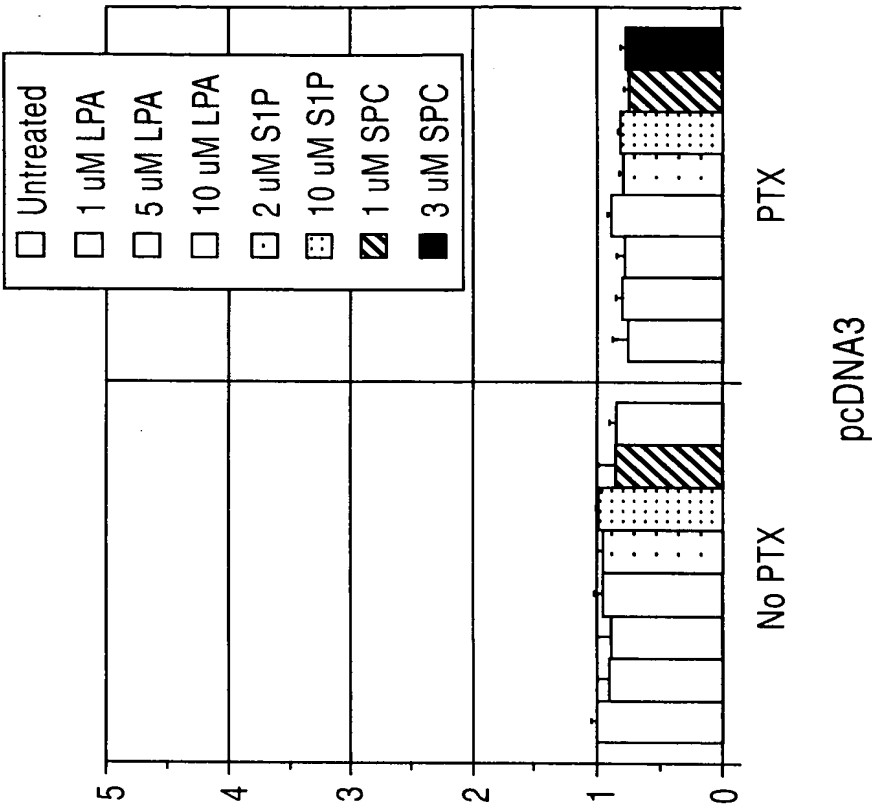
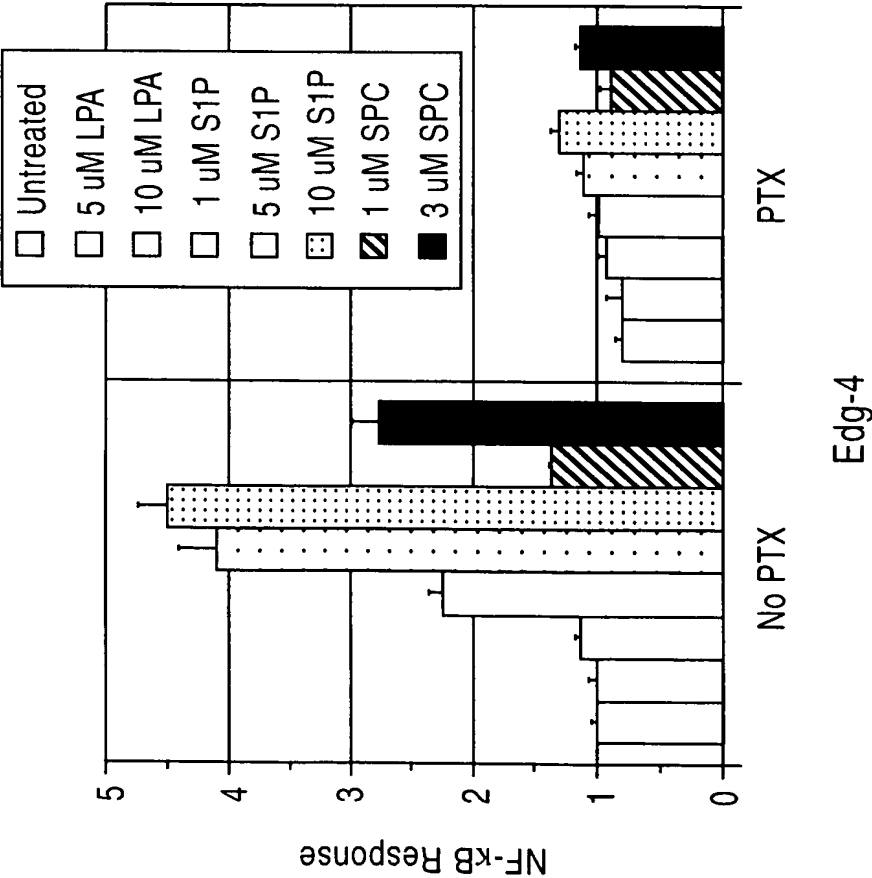


Fig.11A



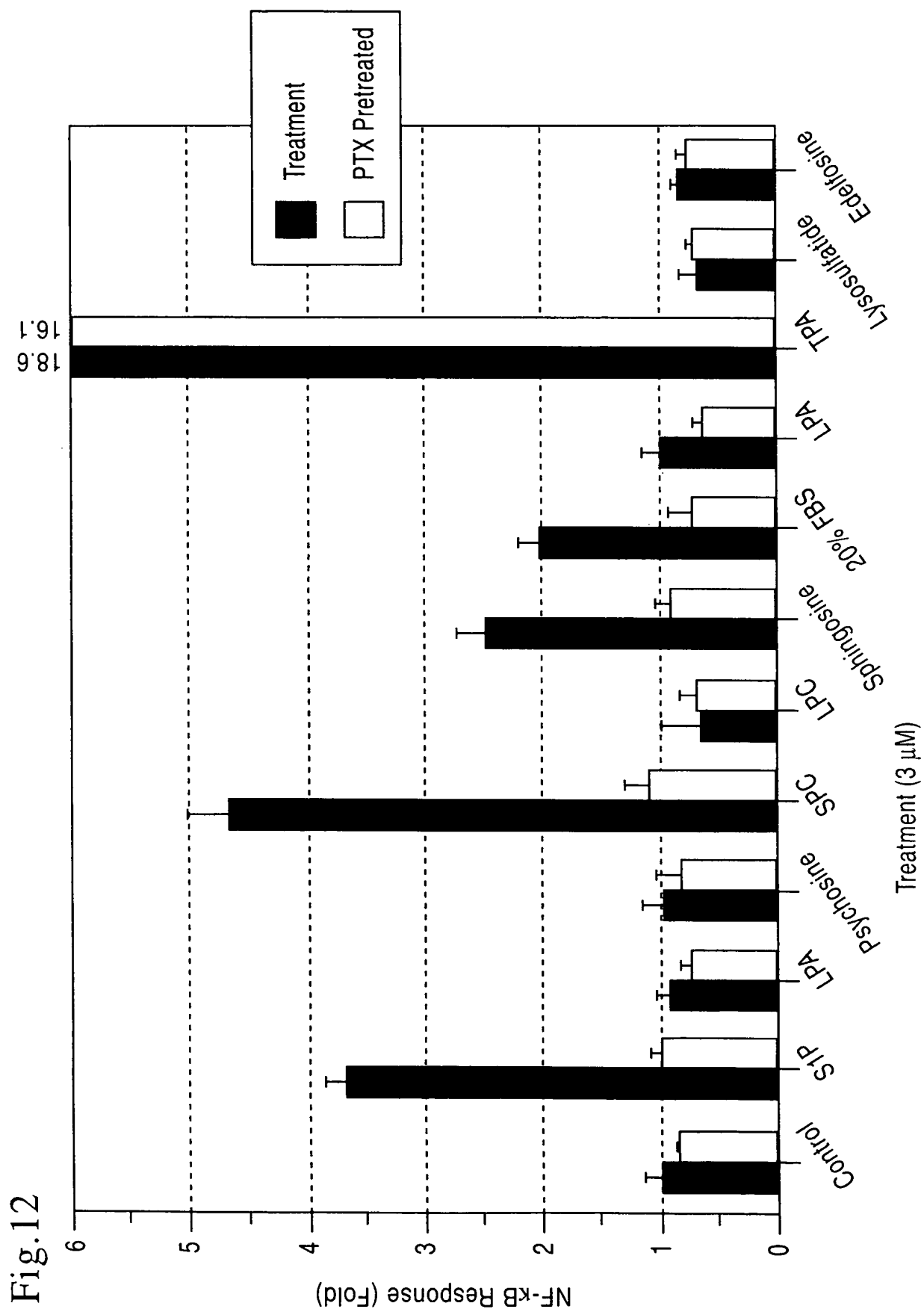




Fig.13B

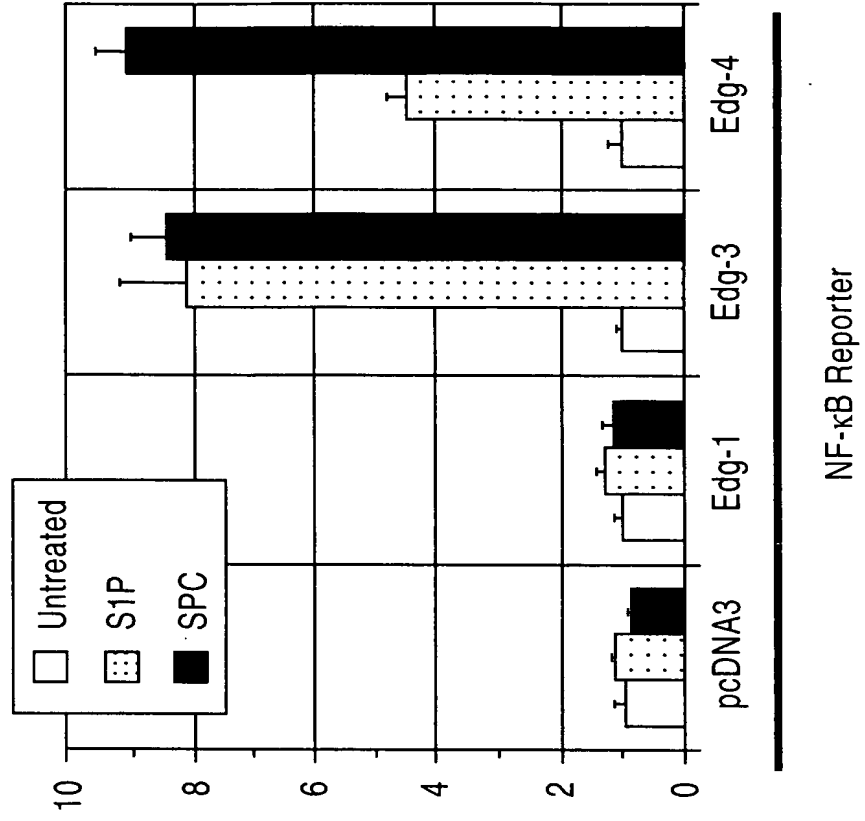


Fig.13A

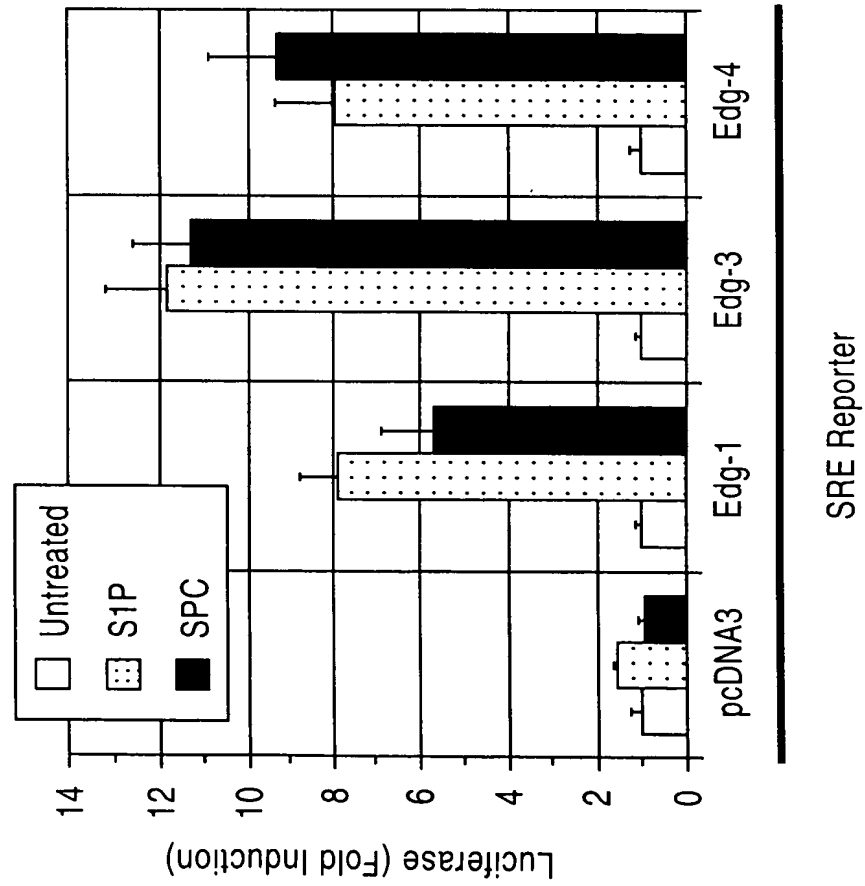


Fig.15A-1

M G S L Y S E Y  
1 AAAGCCCCATGGCCCCAGCAGGCCTCTGAGCCCCACCATGGGCAGCTTGTACTCGGAGTA 60  
-----+-----+-----+-----+-----+-----+  
TTTCGGGGTACCGGGTCTCGGAGACTCGGGTGGTACCCGTGGAACATGAGCCTCAT  
L N P N K V Q E H Y N Y T K E T L E T Q  
61 CCTGAACCCCAACAAGGTCCAGGAACACTATAATTATACCAAGGAGACGCTGGAAACGCA 120  
-----+-----+-----+-----+-----+-----+  
GGACTTGGGGTTGTTCCAGGTCCTTGTGATATTAATATGGTTCCTCTGCGACCTTTGCGT  
E T T S R Q V A S A F I V I L C C A I V  
121 GGAGACGACCTCCCGCCAGGTGGCCTCGGCCTTCATCGTCATCCTCTGTTGCGCCATTGT 180  
-----+-----+-----+-----+-----+-----+  
CCTCTGCTGGAGGGCGGTCCACCGGAGCCGGAAGTAGCAGTAGGAGACAACGCGGTAACA  
V E N L L V L I A V A R N S K F H S A M  
181 GGTGGAACCTTCTGGTGCTCATTGCGGTGGCCCGAAACAGCAAGTTCCTACTCGGCAAT 240  
-----+-----+-----+-----+-----+-----+  
CCACCTTTTGAAGACCACGAGTAACGCCACCGGGCTTTGTGCTTCAAGGTGAGCCGTTA  
Y L F L G N L A A S D L L A G V A F V A  
241 GTACCTGTTTCTGGGCAACCTGGCCGCCTCCGATCTACTGGCAGGCGTGGCCTTCGTAGC 300  
-----+-----+-----+-----+-----+-----+  
CATGGACAAAGACCCGTTGGACCGGCGGAGGCTAGATGACCGTCCGCACCGGAAGCATCG  
N T L L S G S V T L R L T P V Q W F A R  
301 CAATACCTTGCTCTCTGGCTCTGTACGCTGAGGCTGACGCCTGTGCAGTGGTTTGCCCG 360  
-----+-----+-----+-----+-----+-----+  
GTTATGGAACGAGAGACCGAGACAGTGCAGTCCGACTCGGACACGTCACCAAACGGGC  
E G S A F I T L S A S V F S L L A I A I  
361 GGAGGGCTCTGCCTTCATCACGCTCTCGGCCTCTGTCTTCAGCCTCCTGGCCATCGCCAT 420  
-----+-----+-----+-----+-----+-----+  
CCTCCCAGACGGAAGTAGTGCGAGAGCCGAGACAGAAGTCGGAGGACCGGTAGCGGTA  
E R H V A I A K V K L Y G S D K S C R M  
421 TGAGCGCCACGTGGCCATTGCCAAGGTCAAGCTGTATGGCAGCGACAAGAGCTGCCGCAT 480  
-----+-----+-----+-----+-----+-----+  
ACTCGCGGTGCACCGGTAACGGTTCAGTTCGACATACCGTCTGCTGTTCTCGACGGCGTA  
L L L I G A S W L I S L V L G G L P I L  
481 GCTTCTGCTCATCGGGCCTCGTGGCTCATCTCGCTGGTCTCGGTGGCCTGCCCATCCT 540  
-----+-----+-----+-----+-----+-----+  
CGAAGACGAGTAGCCCCGGAGCACCGAGTAGAGCGACCAGGAGCCACCGACGGGTAGGA  
G W N C L G H L E A C S T V L P L Y A K  
541 TGGCTGGAACCTGCCTGGGCCACCTCGAGGCCTGCTCCTGCTGCTCTCTACGCCAA 600  
-----+-----+-----+-----+-----+-----+  
ACCGACCTTGACGGACCCGGTGGAGCTCCGGACGAGGTGACAGGACGGAGAGATGCGGTT  
H Y V L C V V T I F S I I L L A I V A L  
601 GCATTATGTGCTGTGCGTGGTGACCATCTTCTCCATCATCCTGTTGGCCATCGTGGCCCT 660  
-----+-----+-----+-----+-----+-----+  
CGTAATACACGACACGCACCACTGGTAGAAGAGGTAGTAGGACAACCGGTAGCACCGGGA

Fig.15A-2

```

      Y V R I Y C V V R S S H A D M A A P Q T
661 GTACGTGCGCATCTACTGCGTGGTCCGCTCAAGCCACGCTGACATGGCCGCCCCGACAGAC
      -----+-----+-----+-----+-----+
      CATGCACGCGTAGATGACGCACCAGGCGAGTTCGGTGC GACTGTACCGGCGGGGCGTCTG
840
      L A L L K T V T I V L G V F I V C W L P
721 GCTAGCCCTGCTCAAGACGGTCACCATCGTGCTAGGCGTCTTTATCGTCTGCTGGCTGCC
      -----+-----+-----+-----+-----+
      CGATCGGGACGAGTTCTGCCAGTGGTAGCACGATCCGCAGAAATAGCAGACGACCGACGG
780
      A F S I L L L D Y A C P V H S C P I L Y
781 CGCCTTCAGCATCCTCCTTCTGGACTATGCCTGTCCCGTCCACTCCTGCCCGATCCTCTA
      -----+-----+-----+-----+-----+
      GCGGAAGTCGTAGGAGGAAGACCTGATACGGACAGGGCAGGTGAGGACGGGCTAGGAGAT
840
      K A H Y X F A V S T L N S L L N P V I Y
841 CAAAGCCCACTACYTTTTTCGCCGTCTCCACCCTGAATTCCCTGCTCAACCCCGTCATCTA
      -----+-----+-----+-----+-----+
      GTTTCGGGTGATGRAAAAGCGGCAGAGGTGGGACTTAAGGGACGAGTTGGGGCAGTAGAT
900
      T W R S R D L R R E V L R P L Q C W R P
901 CACGTGGCGCAGCCGGGACCTGCGGCGGGAGGTGCTTCGGCCGCTGCAGTGCTGGCGGCC
      -----+-----+-----+-----+-----+
      GTGCACCGCGTCGGCCCTGGACGCGCCCTCCACGAAGCCGGCGACGTNACGACCGCCGG
960
      G V G V Q G R R R G G T P G H H L L P L
961 GGGGGTGGGGGTGCAAGGACGGAGGCGGGGCGGGACCCCGGGCCACCACCTCCTGCCACT
      -----+-----+-----+-----+-----+
      CCCCCACCCCACTTCTGCCTCCGCCCCGCCCTGGGGCCCGGTGGTGGAGGACGGTGA
1020
      R S S S S L E R G M H M P T S P T F L E
1021 CCGCAGCTCCAGCTCCCTGGAGAGGGGCGATGCACATGCCACGTCACCCACGTTTCTGGA
      -----+-----+-----+-----+-----+
      GGCCTCGAGGTGAGGGACCTCTCCCCGTACGTGTACGGGTGCAGTGGGTGAAAAGACCT
1080
      G N T V V *
1081 GGGCAACACGGTGGTCTGAGGGTGGGGGTGGACCAACAACCAGGCCAGGGCATAGGGGTT
      -----+-----+-----+-----+-----+
      CCCGTTGTGCCACCAGACTCCCACCCCCACCTGGTTGTTGGTCCGGTCCCGTATCCCCAA
1140
      CATGGAAAGGCCACTGGGTGACCCCAAATA
1141 -----+-----+-----+ 1170
      GTACCTTCCGGTGACCCACTGGGGTTTAT
```

Fig.15B-1

cDNA sequence of clone pC3-hedg4#36 encoding functional HEDG4 receptor protein.

```

1  ATGGGCAGCTTGTACTCGGAGTACCTGAACCCCAACAAGGTCAGGAACACTATAATTAT  60
   -----+-----+-----+-----+-----+-----+
   TACCCGTCGAACATGAGCCTCATGGACTTGGGGTTGTTCCAGGTCCTTGTGATATTAATA

61  ACCAAGGAGACGCTGGAAACGCAGGAGACGACCTCCCGCCAGGTGGCCTCGGCCTTCATC  120
   -----+-----+-----+-----+-----+-----+
   TGGTTCCTCTGCGACCTTTGCGTCCTCTGCTGGAGGGCGGTCCACCGGAGCCGGAAGTAG

121  GTCATCCTCTGTTGCGCCATTGTGGTGGAAAACCTTCTGGTGCTCATTGCGGTGGCCCGA  180
   -----+-----+-----+-----+-----+-----+
   CAGTAGGAGACAACGCGGTAACACCACCTTTTGAAGACCACGAGTAACGCCACCGGGCT

181  AACAGCAAGTTCCTACTCGGCAATGTACCTGTTTCTGGGCAACCTGGCCGCCTCCGATCTA  240
   -----+-----+-----+-----+-----+-----+
   TTGTCGTTCAAGGTGAGCCGTTACATGGACAAAGACCCGTTGGACCGGCGGAGGCTAGAT

241  CTGGCAGGCGTGGCCTTCGTAGCCAATACCTTGCTCTCTGGCTCTGTACGCTGAGGCTG  300
   -----+-----+-----+-----+-----+-----+
   GACCGTCCGCACCGGAAGCATCGGTTATGGAACGAGAGACCGAGACAGTGCGACTCCGAC

301  ACGCCTGTGCAGTGGTTTGCCCGGGAGGGCTCTGCCTTCATCACGCTCTCGGCCTCTGTC  360
   -----+-----+-----+-----+-----+-----+
   TGCGGACACGTCACCAAACGGGCCCTCCCGAGACGGAAGTAGTGCGAGAGCCGGAGACAG

361  TTCAGCCTCCTGGCCATCGCCATTGAGCGCCACGTGGCCATTGCCAAGGTCAAGCTGTAT  420
   -----+-----+-----+-----+-----+-----+
   AAGTCGGAGGACCGGTAGCGGTAACCTCGCGGTGCACCGGTAACGGTTCAGTTCGACATA

421  GGCAGCGACAAGAGCTGCCGCATGCTTCTGCTCATCGGGGCCCTCGTGGCTCATCTCGCTG  480
   -----+-----+-----+-----+-----+-----+
   CCGTCGCTGTTCTCGACGGCGTACGAAGACGAGTAGCCCCGGAGACCGAGTAGAGCGAC

481  GTCCTCGGTGGCCTGCCCATCCTTGGCTGGAACCTGCCTGGGCCACCTCGAGGCCTGCTCC  540
   -----+-----+-----+-----+-----+-----+
   CAGGAGCCACCGGACGGGTAGGAACCGACCTTGACGGACCCGGTGGAGCTCCGGACGAGG

541  ACTGTCTCGCTCTCTACGCCAAGCATTATGTGCTGTGCGTGGTGACCATCTTCTCCATC  600
   -----+-----+-----+-----+-----+-----+
   TGACAGGACGGAGAGATGCGGTTTCGTAATACAGACACGCACCACTGGTAGAAGAGGTAG

601  ATCCTGTTGGCCGTCGTGGCCCTGTACGTGCGCATCTACTGCGTGGTCCGCTCAAGCCAC  660
   -----+-----+-----+-----+-----+-----+
   TAGGACAACCGGCAGCACCGGGACATGCACGCGTAGATGACGCACCAGGCGAGTTCGGTG

661  GCTGACATGGCCGCCCCGACAGCCTAGCCCTGCTCAAGACGGTCACCATCGTGCTAGGC  720
   -----+-----+-----+-----+-----+-----+
   CGACTGTACC GGCGGGGCGTCTGCGATCGGGACGAGTTCTGCCAGTGGTAGCACGATCCG

721  GTCTTTATCGTCTGCTGGCTGCCCCGCTTCAGCATCCTCCTTCTGGACTATGCCTGTCCC  780
   -----+-----+-----+-----+-----+-----+

```

Fig.15B-2

```
CAGAAATAGCAGACGACCGACGGGCGGAAGTCGTAGGAGGAAGACCTGATACGGACAGGG
781  GTCCACTCCTGCCCAGATCCTCTACAAAGCCCACTACCTTTTCGCCGTCTCCACCCTGAAT 840
-----+-----+-----+-----+-----+-----+
CAGGTGAGGACGGGCTAGGAGATGTTTCGGGTGATGGAAAAGCGGCAGAGGTGGGACTTA
841  TCCCTGCTCAACCCCGTCATCTACACGTGGCGCAGCCGGGACCTGCGGCGGGAGGTGCTT 900
-----+-----+-----+-----+-----+-----+
AGGGACGAGTTGGGGCAGTAGATGTGCACCGCGTCGGCCCTGGACGCCGCCCTCCACGAA
901  CGGCCGCTGCAGTGCTGGCGGCCGGGGTGGGGGTGCAAGGACGGAGGCGGGGCGGGACC 960
-----+-----+-----+-----+-----+-----+
GCCGGCGACGTACGACCGCCGGCCCCCACCCTTCCTGCCTCCGCCCCGCCCTGG
961  CCGGGCCACCACCTCCTGCCACTCCGCAGCTCCAGCTCCCTGGAGAGGGGCATGCACATG 1020
-----+-----+-----+-----+-----+-----+
GGCCCGGTGGTGGAGGACGGTGAGGCGTCGAGGTGAGGGACCTCTCCCCGTACGTGTAC
1021 CCCACGTCACCCACGTTTCTGGAGGGCAACACGGTGGTCTGA 1062
-----+-----+-----+-----+
GGGTGCAGTGGGTGCAAAGACCTCCCGTTGTGCCACCAGACT
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Fig.19

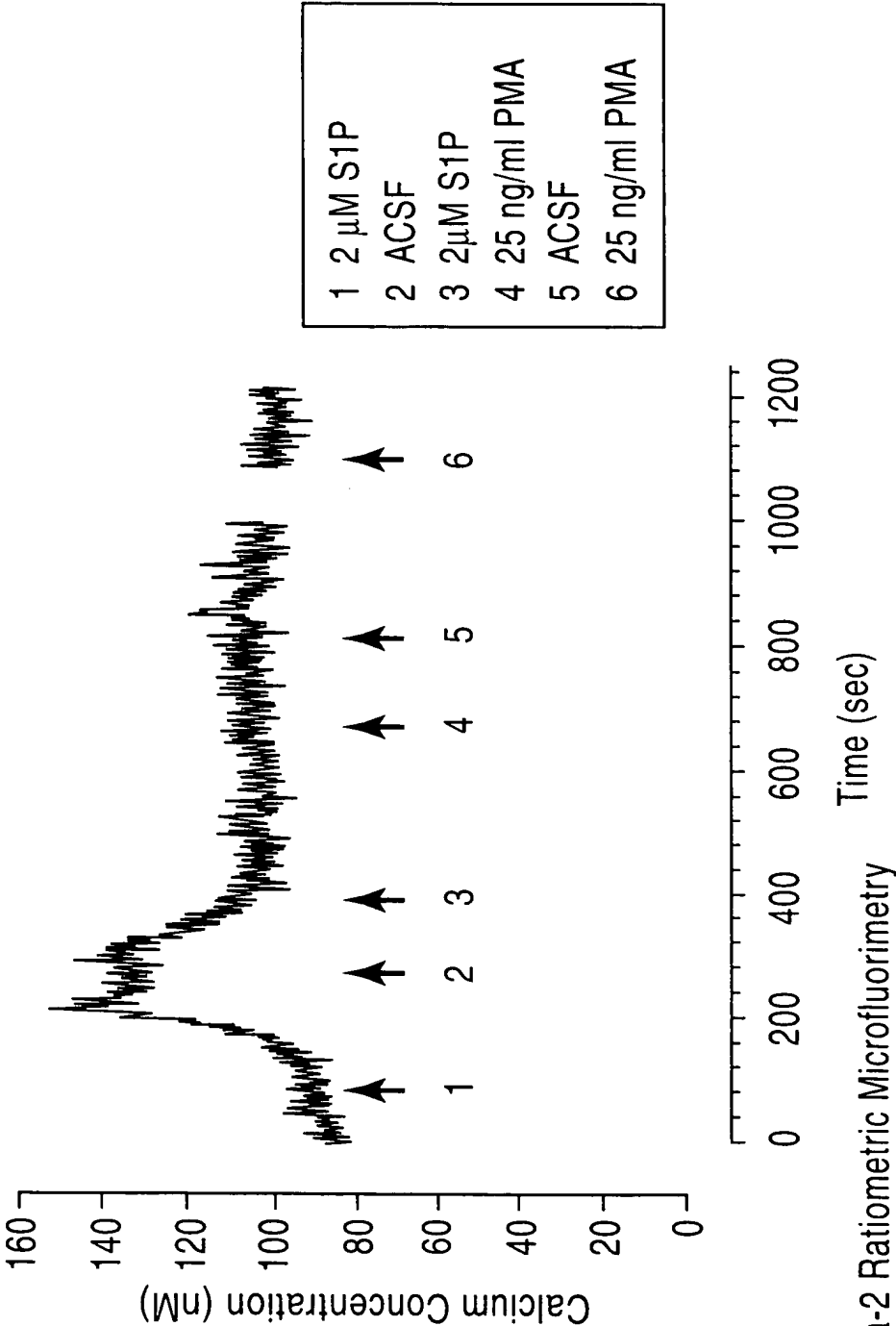
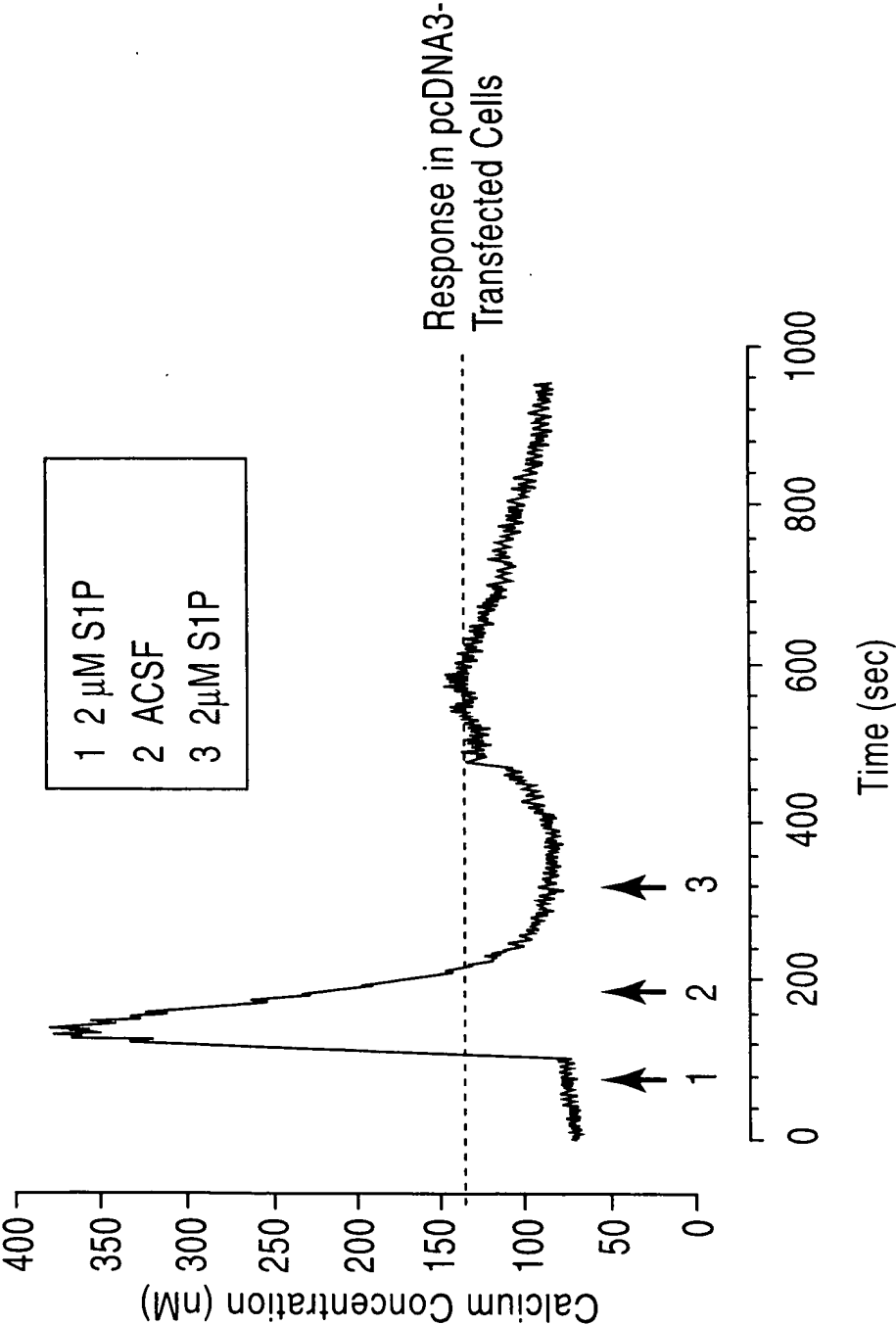


Fig.20



## Fig.22A

### Human Edg-6 Sequence

```

1  ATGGTCATCATGGGCCAGTGCTACTACAACGAGACCATCGGCTTCTTCTATAACAACAGT  60
   -----+-----+-----+-----+-----+-----+
   TACCAGTAGTACCCGGTCACGATGATGTTGCTCTGGTAGCCGAAGAAGATATTGTTGTCA

61  GGCAAAGAGCTCAGCTCCCACTGGCGGCCCAAGGATGTGGTCGTGGTGGCACTGGGGCTG  120
   -----+-----+-----+-----+-----+-----+
   CCGTTTCTCGAGTCGAGGGTGACCGCCGGGTTCTACACCAGCACCACCGTGACCCCGAC

121 ACCGTCAGCGTGCTGGTGCTGCTGACCAATCTGCTGGTCATAGCAGCCATCGCCTCCAAC  180
   -----+-----+-----+-----+-----+-----+
   TGGCAGTCGCACGACCACGACGACTGGTTAGACGACCAGTATCGTCGGTAGCGGAGGTTG

181 CGCCGCTTCCACCAGCCCATCTACTACCTGCTCGGCAATCTGGCCGCGGCTGACCTCTTC  240
   -----+-----+-----+-----+-----+-----+
   GCGGCGAAGGTGGTCGGGTAGATGATGGACGAGCCGTTAGACCGGCGCCGACTGGAGAAG

241 GCGGGCGTGGCCTACCTCTTCTCATGTTCCACACTGGTCCCCGCACAGCCGACTTTCA  300
   -----+-----+-----+-----+-----+-----+
   CGCCCGCACCGGATGGAGAAGGAGTACAAGGTGTGACCAGGGGCGTGTGCGGGCTGAAAGT

301 CTTGAGGGCTGGTTCCTGCGGCAGGGCTTGCTGGACACAAGCCTCACTGCGTCGGTGGCC  360
   -----+-----+-----+-----+-----+-----+
   GAACTCCCGACCAAGGACGCCGTCCCGAACGACCTGTGTTGAGAGTGACGCAGCCACCGG

361 ACACTGCTGGCCATCGCCGTGGAGCGGCACCGCAGTGTGATGGCCGTGCAGCTGCACAGC  420
   -----+-----+-----+-----+-----+-----+
   TGTGACGACCGGTAGCGGCACCTCGCCGTGGCGTCACACTACCGGCACGTGACGTGTGCG

421 CGCCTGCCCCGTGGCCGCGTGGTCATGCTCATTGTGGGCGTGTGGGTGGCTGCCCTGGGC  480
   -----+-----+-----+-----+-----+-----+
   GCGGACGGGGCACC GGCGCACCAAGTACGAGTAACACCCGCACACCCACCGACGGGACCCG

481 CTGGGGCTGCTGCCTGCCCACTCCTGGCACTGCCTCTGTGCCCTGGACCGCTGCTCACGC  540
   -----+-----+-----+-----+-----+-----+
   GACCCCGACGACGGACGGGTGAGGACCGTGACGGAGACACGGGACCTGGCGACGAGTGCG

541 ATGGCACCCCTGCTCAGCCGCTCCTATTTGGCCGTCTGGGCTCTGTGAGCCTGCTTGTC  600
   -----+-----+-----+-----+-----+-----+
   TACCGTGGGGACGAGTCGGCGAGGATAAACCGGCAGACCCGAGACAGCTCGGACGAACAG

601 TTCCTGCTCATGGTGGCTGTGTACACCCGCATTTTCTTCTACGTGCGGCGGCGAGTGACG  660
   -----+-----+-----+-----+-----+-----+
   AAGGACGAGTACCACCGACACATGTGGGCGTAAAAGAAGATGCACGCCGCCGCTCACGTC

661 CGCATGGCAGAGCATGTGAGCTGCCACCCCGCTACCGAGAGACCACGCTCAGCCTGGTC  720
   -----+-----+-----+-----+-----+-----+
   GCGTACCGTCTCGTACAGTCGACGGTGGGGGCGATGGCTCTCTGGTGCGAGTCGGACCAG

721 AAGACTGTTGTATCATCCTGGGGGCGTTCGTGGTCTGCTGGACACCAGGCCAGGTGGTA  780
   -----+-----+-----+-----+-----+-----+
   TTCTGACAACAGTAGTAGGACCCCCGCAAGCACCAGACGACCTGTGGTCCGGTCCACCAT

781 CTGCTCCTGGATGGTTTAGGCTGTGAGTCCTGCAATGTCTGGCTGTAGAAAAGTACTTC  840
   -----+-----+-----+-----+-----+-----+
   GACGAGGACCTACCAAATCCGACACTCAGGACGTTACAGGACCGACATCTTTTCATGAAG
```



Fig.22B

```
CTACTGcTGGCCGAGGCCAACTCACTGGTCAATGCTGCTGTGTACTCTTGCCGAGATGCT
841 -----+-----+-----+-----+-----+-----+-----+ 900
GATGACgACCGGCTCCGGTTGAGTGACCAGTTACGACGACACATGAGAACGGCTCTACGA

GAGATGCGCCGCACCTTCCGCCGCCTTCTCTGCTGCGCGTGCCTCCGCCAGTCCACCCGC
901 -----+-----+-----+-----+-----+-----+-----+ 960
CTCTACGCGGCGTGGAAGGCGGCGGAAGAGACGACGCGCACGGAGGCGGTCAGGTGGGCG

GAGTCTGTCCACTATACATCCTCTGCCCAGGGAGGTGCCAGCACTCGCATCATGCTTCCC
961 -----+-----+-----+-----+-----+-----+-----+ 1020
CTCAGACAGGTGATATGTAGGAGACGGGTCCCTCCACGGTCGTGAGCGTAGTACGAAGGG

GAGAACGGCCACCCACTGATGGACTCCACCCCTTTAG
1021 -----+-----+-----+-----+-----+-----+ 1056
CTCTTGCCGGTGGGTGACTACCTGAGGTGGGAAATC
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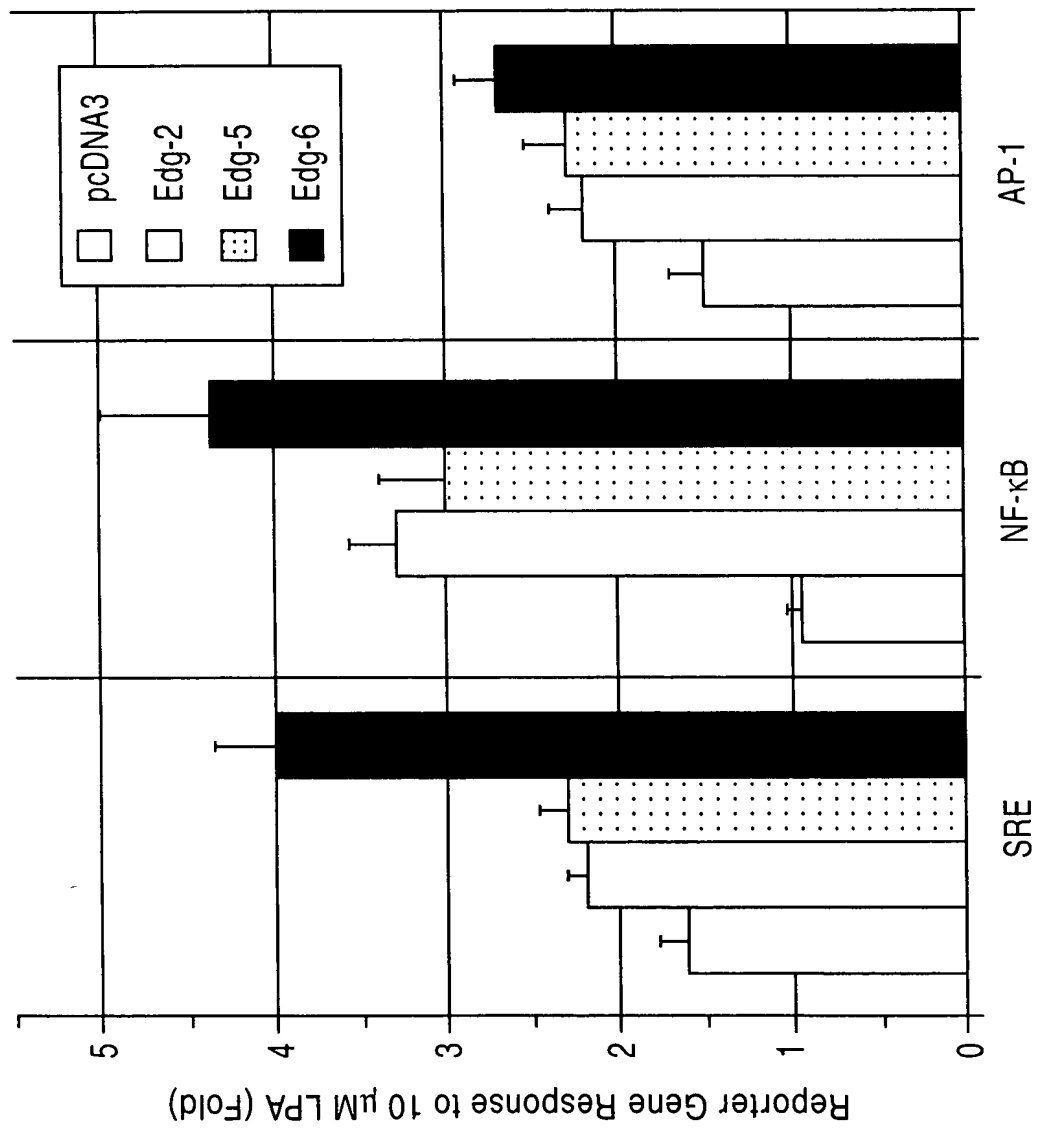


Fig.23

Fig.24

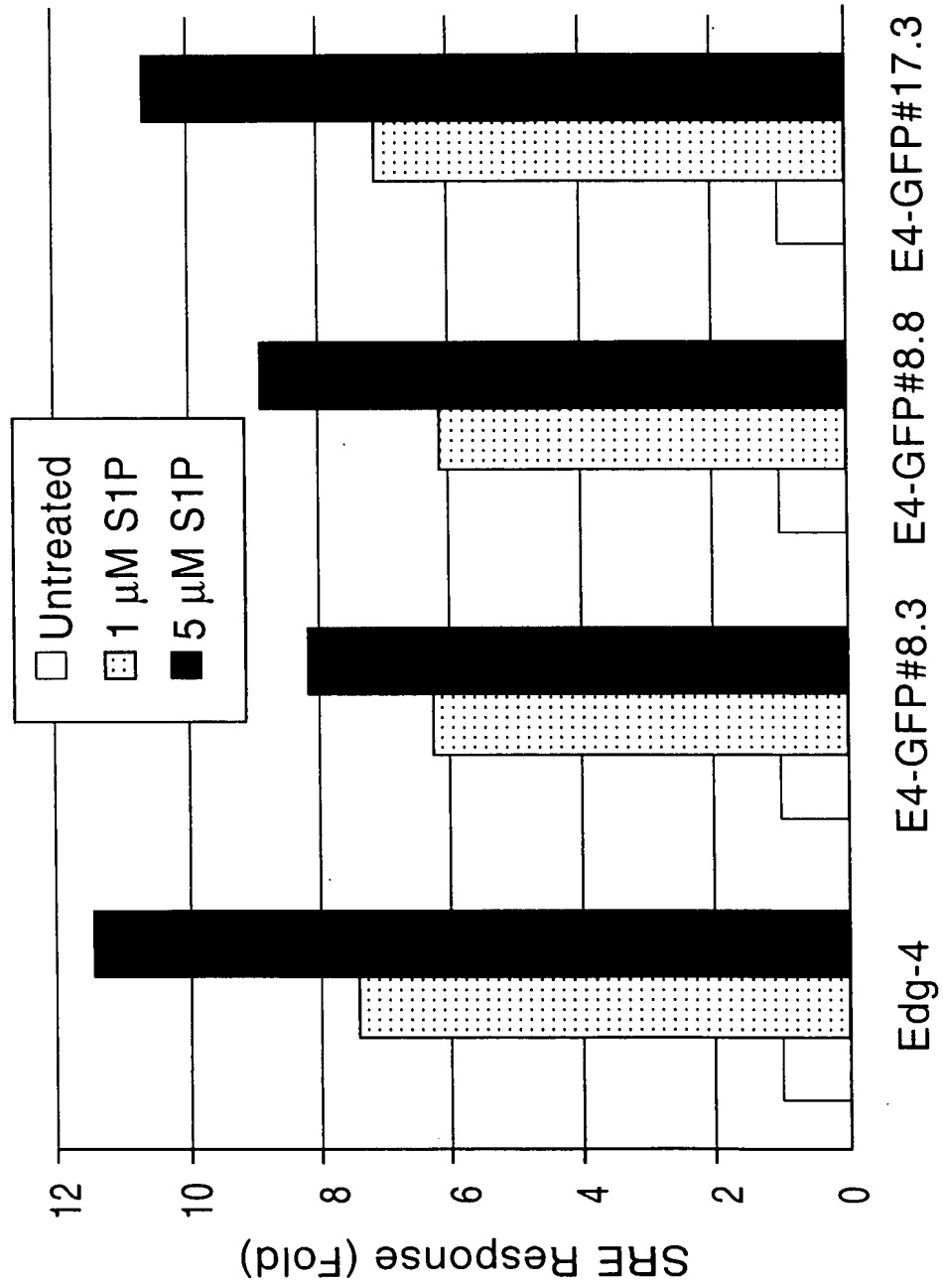
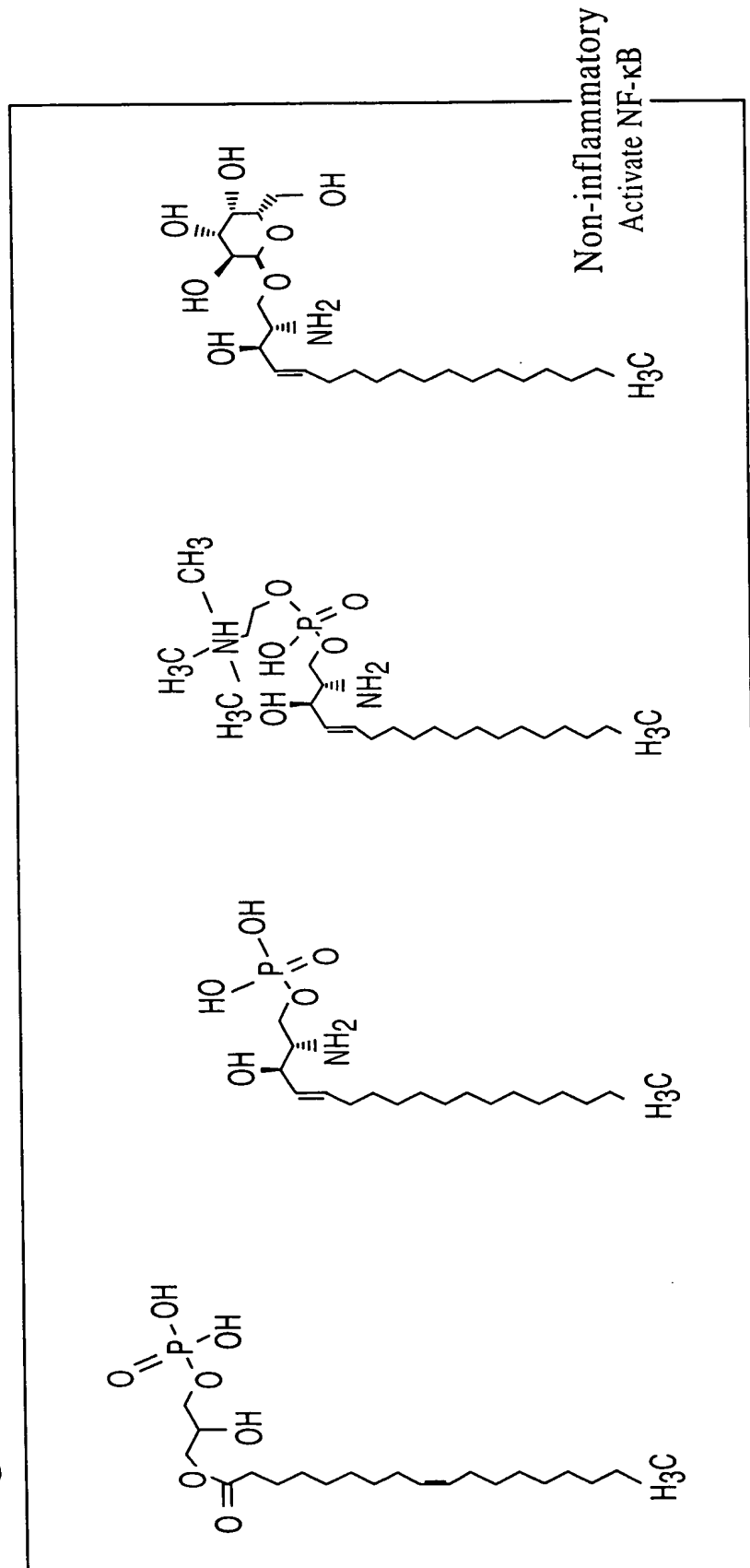


Fig.25



Psychosine

Edg-3  
Edg-4

SPC

Edg-1  
Edg-3  
Edg-4  
Edg-7

S1P

Edg-1  
Edg-3  
Edg-4  
Edg-7

LPA

Edg-2  
Edg-5  
Edg-6